

Understanding the Immune System and Lymphoma

The body's immune system is comprised of a network of cells, tissues, and organs. This network operates together to eliminate harmful pathogens, like bacteria and viruses, as well as cancer cells from the body.

The immune system provides two different types of immunity:

- **Innate** (meaning “inborn” or “natural”) immunity — This type of immunity is provided by natural barriers in the body, substances in the blood, and specific cells that attack and kill foreign cells. Examples of natural barriers include skin, mucous membranes, stomach acid, and the cough reflex. These barriers keep germs (bacteria or viruses) and other harmful substances from entering the body. Inflammation (redness and swelling) is also a type of innate immunity. Blood cells that are part of the innate immune system include neutrophils, macrophages, eosinophils, and basophils.
- **Adaptive** (meaning adapting to external forces or threats) immunity — This type of immunity is provided by the thymus gland, spleen, tonsils, bone marrow, circulatory system, and lymphatic system. B cells and T cells, the two main types of lymphocytes, carry out the adaptive immune response by recognizing and either inactivating or killing specific invading organisms. The adaptive immune system can then “remember” the identity of the invader, so that the next time the body is infected by the same invader, the immune response will develop more quickly and strongly.

All normal cells have a limited lifespan. A self-destruct mechanism called apoptosis is triggered when cells become senescent (too old) or get damaged; this natural process is called apoptosis or programmed sequence of events that lead to the cell's death. However, sometimes damage to the genetic material (DNA) of a cell gives it the ability to override this self-destruct mechanism and allows the cell to continue to live and grow indefinitely, making the cell “immortal” in many ways. Unless the body's immune system gets rid of these abnormal cells, they can become cancerous. In many cancers, including lymphoma, the immune system doesn't work properly, which allows the cancer cells to grow and spread.

THREE MAIN CLASSES OF BLOOD CELLS

Red blood cells (or erythrocytes)

- Red blood cells carry oxygen from the lungs to all the tissues in the body. Red blood cells also remove the carbon dioxide waste produced by cells and bring it to the lungs to be exhaled. A low number of red blood cells is called anemia. A person with anemia may feel tired, weak, and/or short of breath.

White blood cells (or leukocytes)

- White blood cells work as part of the immune system to help the body fight infections.

The main types of white blood cells are:

- **Lymphocytes** — These are discussed on the following page.
- **Granulocytes** — There are three types of granulocytes: neutrophils, basophils, and eosinophils. Neutrophils help fight bacterial infections. A low number of neutrophils in the blood is called neutropenia. People with neutropenia are more likely to get infections (mostly bacterial infections) than people with normal numbers of neutrophils. Basophils are cells that take part in inflammatory reactions. Eosinophils also help fight infections — particularly those caused by parasites — and they can become plentiful during allergic reactions.
- **Monocytes** — These also play an important role in immunity and are usually the first cells to recover after an episode of neutropenia.

Platelets (or thrombocytes)

- Platelets are cell fragments produced by cells in the bone marrow. They can stop bleeding from broken blood vessels by sticking together to form a blood clot. A low number of platelets is called thrombocytopenia. People with thrombocytopenia are more likely to bruise and bleed with minor trauma. They are also more likely to have severe and recurring nosebleeds and bleeding gums.

Because blood cells have a limited lifespan, the body needs to constantly replenish its supply of these cells. The average red blood cell lives for about 120 days; most white blood cells have a much shorter lifespan, ranging from a few hours to a few weeks. New blood cells are made by hematopoietic (blood-forming) stem cells, which are immature (non-specialized) cells that can develop into any kind of blood cell. Hematopoietic stem cells are found mainly in the bone marrow (the spongy, fatty material inside large bones such as the pelvis, vertebrae, and ribs).

Although, the white blood cells are the only class of blood cells that are a part of the immune system, it is important to understand that red blood cells and platelets play an important role in monitoring an individual's health.

LYMPHOMA AND THE IMMUNE SYSTEM

Lymphoma is a cancer that starts in a lymphocyte, a type of white blood cell. These white blood cells work together with other cells in the immune system to defend the body. Lymph nodes are part of the lymphatic system and typically are the sites in which the body develops an immune response to viruses and bacterial infections. There are three main types of lymphocytes:

- B lymphocytes (B cells) — B cells make antibodies to fight infections.
- T lymphocytes (T cells) — There are many types of T cells. Some help B cells make antibodies, some attack and kill infected cells, and others help control or regulate the way other parts of the immune system fight infections.
- Natural killer (NK) cells — NK cells attack and kill cancer cells and virus-infected cells.

An important component to the body's immune system are immunoglobulins, also known as antibodies. Immunoglobulins are proteins that are produced by B cells. Immunoglobulins recognize and attack particular antigens (cell markers or other proteins) by sticking to viruses, bacteria, or other foreign substances in the body.

IMMUNOGLOBULINS A, G AND M

There are 5 major classes of immunoglobulins: IgG, IgM, IgA, IgD, and IgE. However, for lymphoma and CLL patients, only two types of immunoglobulins are closely monitored:

- Immunoglobulin G (IgG) are the most abundant type of antibody that are found in the body's fluids. IgG is the body's main defense against virus or bacteria.
- Immunoglobulin M (IgM) circulates throughout the blood and helps fight infections.

MONITORING IMMUNOGLOBULIN LEVELS

Since lymphoma/CLL are cancers that affect B cells, it is important to monitor immunoglobulin levels. A blood test can determine the status of the body's immunoglobulin levels and the body's ability to fight off harmful pathogens. Blood tests, age, overall health and other factors can help health care providers determine the best treatment options for a particular patient.

If a blood test result shows low IgG levels, the body's immune system may have a weakened ability to fight infections, especially bacterial ones. A patient can receive intravenous immunoglobulin, or IVIG. When receiving IVIG, the patient receives pooled antibodies from a number of donors, typically once a month, to help the body fight infections. A high level of IgG may mean an active chronic infection, or it may be associated with a lymphoid malignancy.

An elevated IgM may be associated with Waldenström macroglobulinemia, a type of Non-Hodgkin lymphoma. Therefore, a blood test is important to monitor IgM levels in these patients. High levels of IgM can cause hyperviscosity (thickening of the blood). When blood thickens, it has trouble moving through blood vessels. Some patients with hyperviscosity experience no symptoms, while others may experience the following: bleeding (particularly of the nose and gums), headaches, dizziness, double vision, fatigue (extreme tiredness), night sweats, pain or numbness in the extremities, and increased size of the liver, spleen, and lymph nodes.

Again, it is important for your health care provider to monitor excess and deficiencies of immunoglobulin levels throughout and beyond treatment.

TREATMENTS

Cancer treatments are designed to help the body fight cancer by identifying antigens on cancer cells. Some treatments utilize the body's own immune system to help fight cancer cells. The term immunotherapy refers to treatments that help boost the body's own immune response. Immunotherapies help the immune system recognize lymphoma cells and eliminate them from the body.

Other treatments introduce antibodies to help the body recognize and fight cancer cells. Treatments can also include monoclonal antibodies, molecules that have been engineered in a laboratory to behave differently than antibodies found naturally in our bodies. Monoclonal antibodies are specifically designed to recognize and stick to a particular antigen on the surface of certain cancer cells. Rituximab (Rituxan) became

the first monoclonal antibody approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with lymphoma.

There are several classes of immunotherapy that are either approved or under investigation to lymphoma patients, including antibody drug conjugates, bispecific antibodies, checkpoint inhibitors, cytokines, and immunomodulatory drugs. For specific drug names and information, see LRF's fact sheet on Immunotherapy and Lymphoma.

Treatment and maintenance therapies can affect your immune system therefore health care providers conduct a complete blood count (CBC). CBC is conducted by taking a small blood sample. This sample is an important method to monitoring red cells, white cells and platelets during and beyond treatment. Consider talking to your health care provider about your immune system and immunoglobulin levels before beginning treatment or maintenance therapy. LRF's publications have more information on specific treatments and lymphoma subtypes. To access these free publications, visit lymphoma.org/publications.

PROTECTING YOURSELF AND YOUR IMMUNE SYSTEM

Striving to maintain a healthy lifestyle or habits when possible can help the immune system. Sleep, moderate exercise and a healthy diet can help an immune system during or after treatment. Talk to your doctor about what diet and exercise is best for you.

It's also important to take steps to protect yourself from infections. A simple way to protect yourself from infections recommended by the Center of Disease Control and Prevention (CDC) is washing your hands. Wash your hands often with soap and water for at least 20 seconds, especially after going to the bathroom; before eating; and after blowing your nose, coughing, or sneezing.

Ask your health care provider how else you can incorporate preventative measures into your daily routine. This is especially important during times when the number viral infection cases increase, like during the flu season. Viral infections, like the flu, can spread easily and people who have chronic medical conditions may be at higher risk to infections. To learn more about how to prevent getting the coronavirus disease, read our COVID-19/Novel Coronavirus: What Patients Need to Know Fact Sheet at lymphoma.org/publications.

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QUESTIONS TO ASK YOUR DOCTOR

The cancer itself and treatment can alter the immune system. Lymphoma/ CLL patients and survivors should consult with their health care provider for more information about monitoring their immunoglobulin levels and how to best protect their immune system. Communicating with all of the members of your health care team will improve the quality of your care. Questions you can consider asking your health care provider to begin this conversation include:

- What steps can I take to protect myself during flu season?
- Does stress, sleep and exercise affect my immune system?
- Should I not get certain vaccines like typhoid, flu, hepatitis and pneumonia?
- Are there vitamins or any supplements that I should or should not take to help boost my immune system?
- How often do I need a blood test to monitor my immunoglobulin levels?

For Patients in Treatment:

- How can I boost my immune system during treatment?
- What are safe exercises for me to do while undergoing treatment?
- Should I consider changing my diet?

It's also important to tell your health care provider (oncologist and primary care physician) about any other health issues or medications you're currently taking. Considering having your questions written out and with you during your appointments.

GLOSSARY

- **B lymphocytes (B cells):** B cells make antibodies to fight infections
- **Center of Disease Control and Prevention (CDC):** Federal body that creates guidelines to protect the health for people and communities through health promotion, prevention of disease, injury and disability, and preparedness for new health threats
- **Immunoglobulin:** Antibodies that circulate throughout the body and protect the body from antigens
- **Immunoglobulin G (IgG):** An antibody that is the first line of defense for the body when fighting a virus or bacteria
- **Immunoglobulin M (IgM):** An antibody that circulates throughout the blood and helps fight infections
- **Intravenous immunoglobulin (IVIG):** When a patient receives antibodies from a donor intravenously (through the vein)
- **Lymphocytes:** A type of white blood cell that work together with other cells in the immune system to defend the body
- **Natural killer (NK) cells:** NK cells attack and kill cancer cells and virus-infected cells
- **T lymphocytes (T cells):** Help B cells make antibodies, some attack and kill infected cells, and others help control or regulate the way other parts of the immune system fight infections
- **U.S. Food and Drug Administration (FDA):** Federal body responsible for closely monitoring and regulating drug manufacturing processes to protect public health

Patient and Caregiver Support Services

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. One-to-one peer support programs, such as LRF's Lymphoma Support Network, connect patients and caregivers with volunteers who have experience with lymphoma/CLL, similar treatments, or challenges, for mutual emotional support and encouragement. Patients and loved ones may find this information useful whether the patient is newly diagnosed, in treatment, or in remission.

Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and CLL, including our award-winning mobile app, *Focus on Lymphoma*. LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts for people living with lymphoma/CLL, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options. For more information about any of these resources, visit our website lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

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